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Heuristics for the Hodgkin–Huxley system ☆

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ABSTRACT

Hodgkin and Huxley (HH) discovered that voltages control ionic currents in nerve membranes. This led them to describe electrical activity in a neuronal membrane patch in terms of an electronic circuit whose characteristics were determined using empirical data. Due to the complexity of this model, a variety of heuristics, including relaxation oscillator circuits and integrate-and-fire models, have been used to investigate activity in neurons, and these simpler models have been successful in suggesting experiments and explaining observations. Connections between most of the simpler models had not been made clear until recently. Shown here are connections between these heuristics and the full HH model. In particular, we study a new model (Type III circuit): It includes the van der Pol-based models; it can be approximated by a simple integrate-and-fire model; and it creates voltages and currents that correspond, respectively, to the h and V components of the HH system.

1. Introduction

A key discovery by Hodgkin and Huxley was that voltages control the dynamics of ionic currents in a nerve membrane [1]. This led them to describe electrical activity on a membrane patch in terms of an electronic circuit. Others had earlier investigated neural behavior using circuits, notably Balthasar van der Pol [2] and Otto Schmitt [3,4]. Their studies and various modifications of them are widely used today in a variety of studies ranging from brain science to quantum computing.

The Hodgkin–Huxley model (HH) [5] has the form

$$\frac{dV}{dt} = g(x)(E(x) - V) \tag{1}$$

$$\frac{dx}{dt} = \alpha(V)(1 - x) - \beta(V)x$$

where

$$x = (m, n, h)^T$$
$$\alpha(V) = \text{diag}\,(\alpha_m(V), \alpha_n(V), \alpha_h(V))$$
$$\beta(V) = \text{diag}\,(\beta_m(V), \beta_n(V), \beta_h(V))$$
$$g = g_{Na} + g_K + g_L$$
$$E = \frac{g_{Na}E_{na} + g_K E_K + g_L E_L}{g}$$

where E_{Na}, E_K, E_L are the resting potentials for respective ions, and $g_{Na} = \bar{g}_{Na} m^3 h, g_K = \bar{g}_K n^4$, and $g_L = \bar{g}_L$ denote channel conductances. Here the $\bar{g}$'s denote constants and the α's and β's are functions derived from empirical data. This system of Eqs. (1) is complicated, but simpler relaxation oscillators and integrate-and-fire models have provided useful heuristics in a variety of studies. How these simpler models may be related to HH is explored here.

B. van der Pol studied two models of interest to neuroscientists: One system is often depicted using a tunnel-diode for an escapement and is designated as the van der Pol-Bonhoeffer–FitzHugh–Nagumo model [6], in various combinations of these names. This is referred to here as being van der Pol's Type II circuit. van der Pol's other model is often overlooked in neuroscience, although Buzsaki [7] and Chua [8] mention it; it was based on a neon bulb (or glow lamp), and it is referred to here as being van der Pol's Type I circuit. It has recently been shown using singular perturbation methods that an integrate-and-fire circuit resides within a Type I circuit [9]. In another thread of the story, Otto Schmitt, working with Hodgkin and Katz in Cambridge, developed a circuit for analog studies of spiking activity. Schmitt's circuit provides a good analog of a simple integrate-and-fire model, and it resulted in development of the Schmitt trigger, which is used throughout electronics today. Type III circuits are obtained here by combining Type I and Type II circuits. Type III circuits yield a favorable numerical comparison with the full HH system, and give analog electronic circuits that are similar to the Morris–Lecar model [10]. These models and their connections are described here.

All of these models, including HH, may be described generically as involving memristic circuit elements, some of which were described by Leon Chua in his prescient work [11]: Recall that Ohm's Law states that the voltage across a resistor is proportional to the current through it ($V = RI$, where the constant R is called the resistance). Chua postulated that in addition to inductors, resistors and

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capacitors, there should be a circuit element that has the characteristic form $V = M(x)I$ where x is some collection of auxiliary variables (related to magnetic flux) and the conduction $M(x)$ has a nonlinear form. Such circuit elements have recently been created and are used in some surprising applications in quantum computing.

2. Integrate-and-fire circuit

An integrate-and-fire circuit is a simple fill-and-flush device. It comprises an applied signal S (volts) in series with a resistor R (ohms) and a capacitor C (farads), but it is confounded by a switch that shorts the capacitor to ground when its voltage hits a specified threshold. The circuit is shown in Fig. 1. Let $V(t)$ denote the voltage observed on the capacitor. Ohm's Law states that the current through the resistor R is

$$I = \frac{S - V}{R},$$

so S and R combine to create a current source for the circuit. Kirchhoff's Law of Currents tells us that this current must balance the current into the capacitor, which is $I_C = C\,dV/dt$, plus the current through the switch, $g(V)V$, where $g(V) = 0$ for $V < V^*$, but $g(V) = g_\infty \gg 1$ if $V \geqslant V^*$. Combining these gives a mathematical description of this RC-circuit when the switch is open in terms of a differential equation

$$\tau \frac{dV}{dt} = S - V,$$

for $V(t)$ where $\tau = RC$ is the system's time constant and S is the system's driving voltage, as long as $V < V^*$.

The mathematical description of the circuit with the switch will be discussed later, but since the current becomes very large in this formulation, the model is often shortened to the equations

$$\tau \frac{dV}{dt} = S - V \quad \text{for } V < V^*, \quad \text{but } V(t) = 0 \quad \text{if } V(t^-) = V^*. \tag{2}$$

A computer solution of this model is shown in Fig. 2. While these voltages do not resemble action potentials, they do describe repetitive firing, and as explained later, may represent the h-component of HH, where an action potential occurs at each reset event.

Analog circuits for the model in Fig. 1 were designed by Otto Schmitt in the 1930's. He was an early biophysicist, and he worked with notable neuroscientists in England, including Katz and Hodgkin, where his implementation was used to study voltage pulses on squid axons. For the escapement represented by $g(V)$ in Fig. 1, he devised what is now called a Schmitt trigger, which is widely used in electronics. It is described in modern terms using a transistor and a voltage comparator. The variable conductance $g(V)$ in Fig. 1 may be modeled using a Schmitt trigger as shown in Fig. 3.

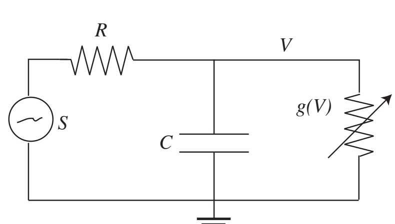

Fig. 1. Integrate-and-fire Circuit. A signal S is applied to the circuit. This creates a current through the resistor R. The symbol $g(V)$ denotes a switch in the circuit that has conductance g - it is essentially a variable resistor. When it is open (not conducting, $g(V) = 0$), the current through R charges the capacitor. When V hits a specified threshold value, say $V = V^*$, the switch closes ($g(V) \gg 1$ for $V > V^*$), causing (almost) instantaneous discharge of the capacitor, thereby resetting V to $V = 0$. After this event, the switch again opens, and the process may be repeated. The result resembles a saw-tooth wave, as shown in Fig. 2.

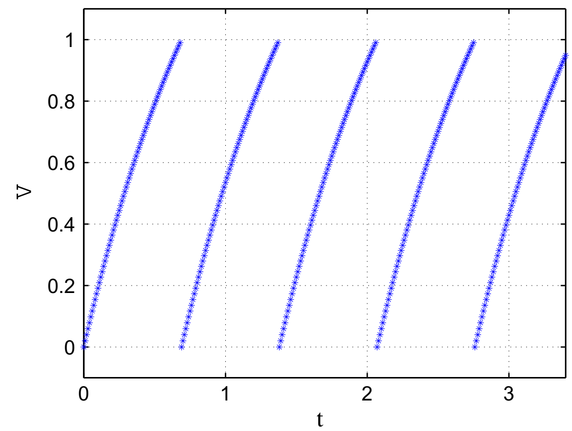

Fig. 2. Voltages generated by the integrate-and-fire model (2) with $S(t) \equiv 2$. A reset event occurs at each instant when V hits $V^* = 1$, and then V is reset to 0. The voltage $V(t)$ tries to follow the input $S(t)$, but is interrupted each time it hits V^*; hence, the oscillation.

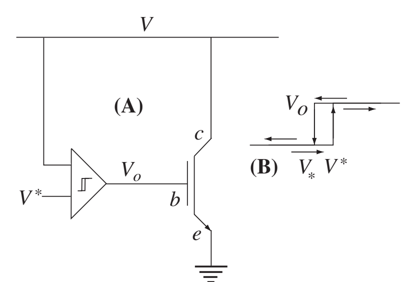

Fig. 3. Modeling $g(V)$ in (3). The switch, denoted by $g(V)$ in Fig. 1, may be constructed using a Schmitt trigger as shown here. Panel (A) depicts the circuit, and Panel (B) depicts how the output voltage (V_0) of the trigger changes with the input voltage V. As the voltage V increases from below V_*, the voltage $V_0 = 0$. When V hits the threshold level V^*, the output voltage V_0 rises, which opens the gate on the transistor (b), allowing a strong current to pass to ground. The output V_0 is hysteretic, meaning that as the voltage V decreases, the output remains high until V hits the lower threshold V_* when the output voltage resets to the lower value $V_0 = 0$.

In summary, we may write the integrate-and-fire model depicted in Fig. 1 in the form

$$\tau \frac{dV}{dt} = S - V - Rg(V)V \tag{3}$$

where it is understood that $g(V)$ becomes very large when V meets or exceeds the threshold $V = V^*$.

3. van der Pol's circuits

Early in the twentieth century B. van der Pol devised and studied two important electronic circuits that have become canonical mathematical models in the literature. The first was based on a neon bulb, that in present times may be replaced by any of a variety of circuit elements. The second was based on a vacuum tube, that in present times is replaced by a tunnel diode. Both of these circuits have interesting connections to neuroscience. Both of them are of the fill-and-flush type, where a capacitor is charged up to a threshold, but each circuit has a different mechanism to quickly discharge the capacitor: In the first, a neon bulb provides high resistance at certain voltages, but low resistance beyond some threshold. In the second case, the tunnel diode behaves like a